Chapter 47 – **ELEMENTS OF BIOLOGY**

Biology is the science of life. The word microbiology refers to the observation of biological systems in the optical (micrometer) size scale. Molecular biology is the science of biology at the molecular level. The new term nanobiology could refer to investigations in the nanometer scale. This is our focus.

1. CELL BIOLOGY

Understanding the cell drives a great deal of biology research. Microbiology is moving from a mode driven by clinical research to new developments in bio-genetics. The human genone has been mapped out a few years ago. The 23 pairs of chromosomes contain DNA which codes for around 23,000 protein-coding genes involving some 3 billion base pairs. These control the synthesis of all proteins. The order of the nucleotides in DNA controls the order of amino acids in protein synthesis. Proteins perform most of the biological functions essential for life (Becker et al, 1999).

Cells contain organelles which perform specific functions. One of these, the nucleus, contains the DNA double helix packed into the chromosomes. The same DNA is contained in every nucleus of every cell in the body. Cell division involves DNA replication whereby new copies are made.

Cells are bounded by a membrane with a hydrophobic interior and a hydrophilic exterior. Lipids are surfactant-like molecules containing (hydrophobic) hydrocarbon tails and polar (hydrophilic) head groups; lipids form the cell membrane. Special proteins help in the transport of essential ingredients into and out of the cell. The passage of small molecules (such as CO_2 and H_2O) and of essential ionic groups also occurs.

The interplay of hydrophobic and hydrophilic interactions is a major diving force in the working of membranes, in the assembly of cellular structures as well as in the folding of macromolecules such as DNA and proteins. Proteins are folded into helical and sheet portions in their active form which is essential for specific functions.

Polysaccharides perform storage and structural functions in cells. Starch and cellulose are typical plant polysaccharides. They are formed of repeating sugar glucose units.

2. LIPIDS

The simplest components of a cell are the lipid molecules forming the membranes. These are amphiphile (surfactant) molecules with hydrophilic head groups and hydrophobic tails. Membranes surround the cell as well as the organelles inside the cell. Proteins form channels across the membrane and other structures in membranes.

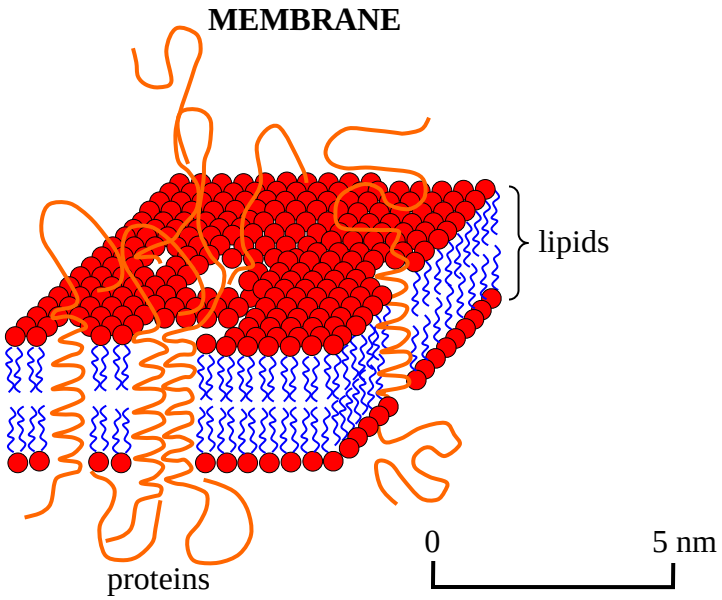

Figure 1: Schematic representation of a membrane.

Lipids are formed from a glycerol backbone and fatty acid side chains. These two undergo a condensation reaction that removes a water molecule.

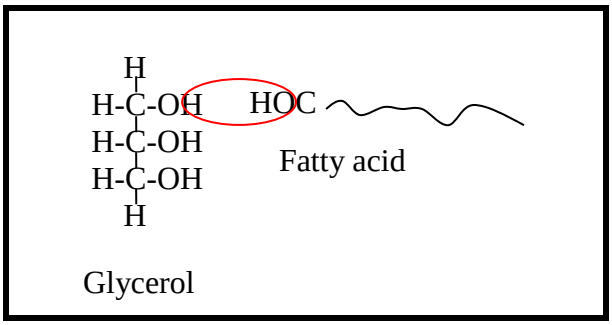

Figure 2: Reaction that forms lipids.

One specific lipid corresponding to a C17 hydrocarbon tail is included here.

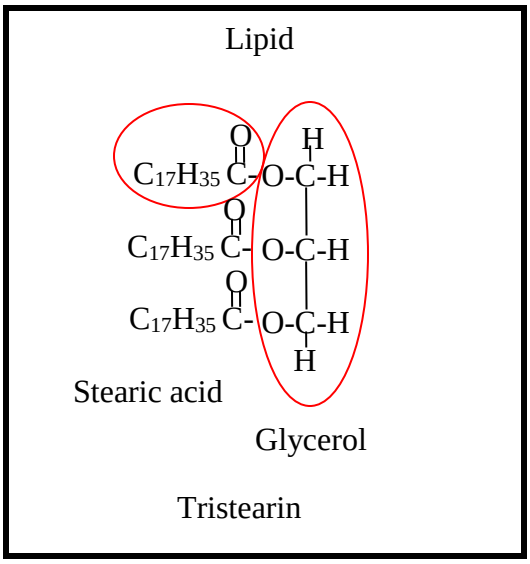

Figure 3: Example of a lipid molecule.

The fatty acids forming the lipid tails contain either C=C double bonds or saturated C-C single bonds. The double bonds produce kinks in the fatty acid chain.

3. DNA AND RNA

DNA is the key component for the passage of genetic information between parent and offspring cells or organisms. It is composed of linear chains of nucleotides, whose sequence determines and regulates subsequent expression of proteins and this, in turn, all phenotype traits. RNA plays an intermediate role in reading the DNA code. Genetic information in the deoxyribonucleic acid (DNA) and the ribonucleic acid (RNA) molecules is identical except for a small difference on the sugar ring. DNA contains deoxyribose whereas RNA contains ribose. The DNA chain is synthesized through a condensation reaction as well.

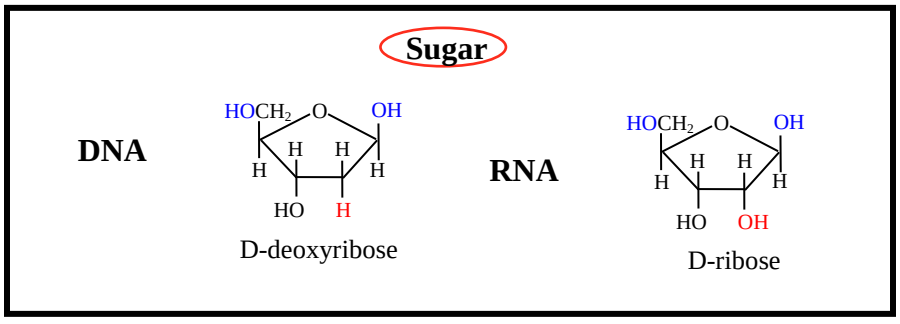

Figure 4: Chemical formula for the sugar ring in DNA and in RNA.

Messenger RNA contains the genetic information (transcribed from DNA) that dictates the amino acid sequence during the synthesis of polypeptides. Transfer RNA brings the correct amino acid to the next site during this synthesis process on ribosomes. RNA is formed of single strands.

Each DNA nucleotide is formed of a phosphate group, a five-carbon sugar, and an amine base. Different nucleotides contain different amine bases. Please note that the DNA chain runs either from the 5' position to the 3' position on the sugar or in the other direction (position 3' to 5').

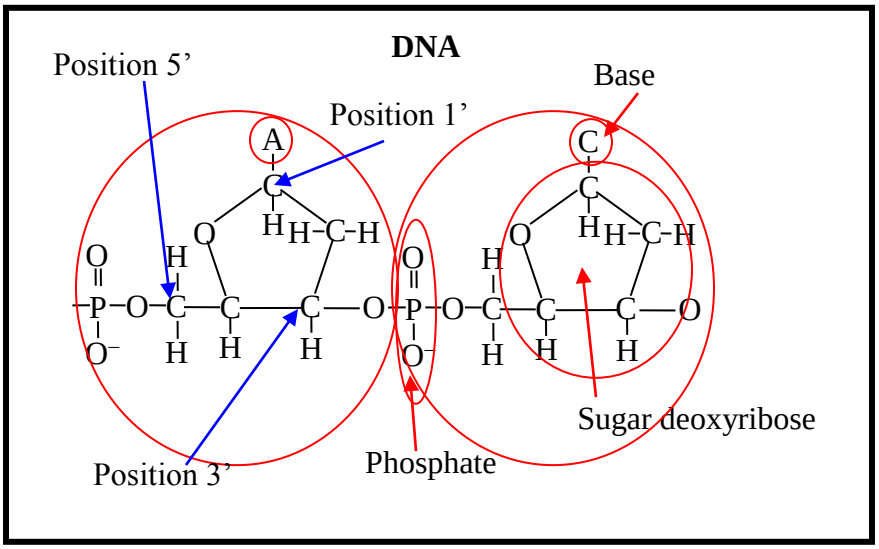

Figure 5: Components of the DNA nucleotide.

There are four amine bases in DNA: Adenine (A), Thymine (T), Guanine (G) and Cytosine (C). In RNA, Thymine (T) is replaced by Uracil (U).

THE DNA MOLECULE

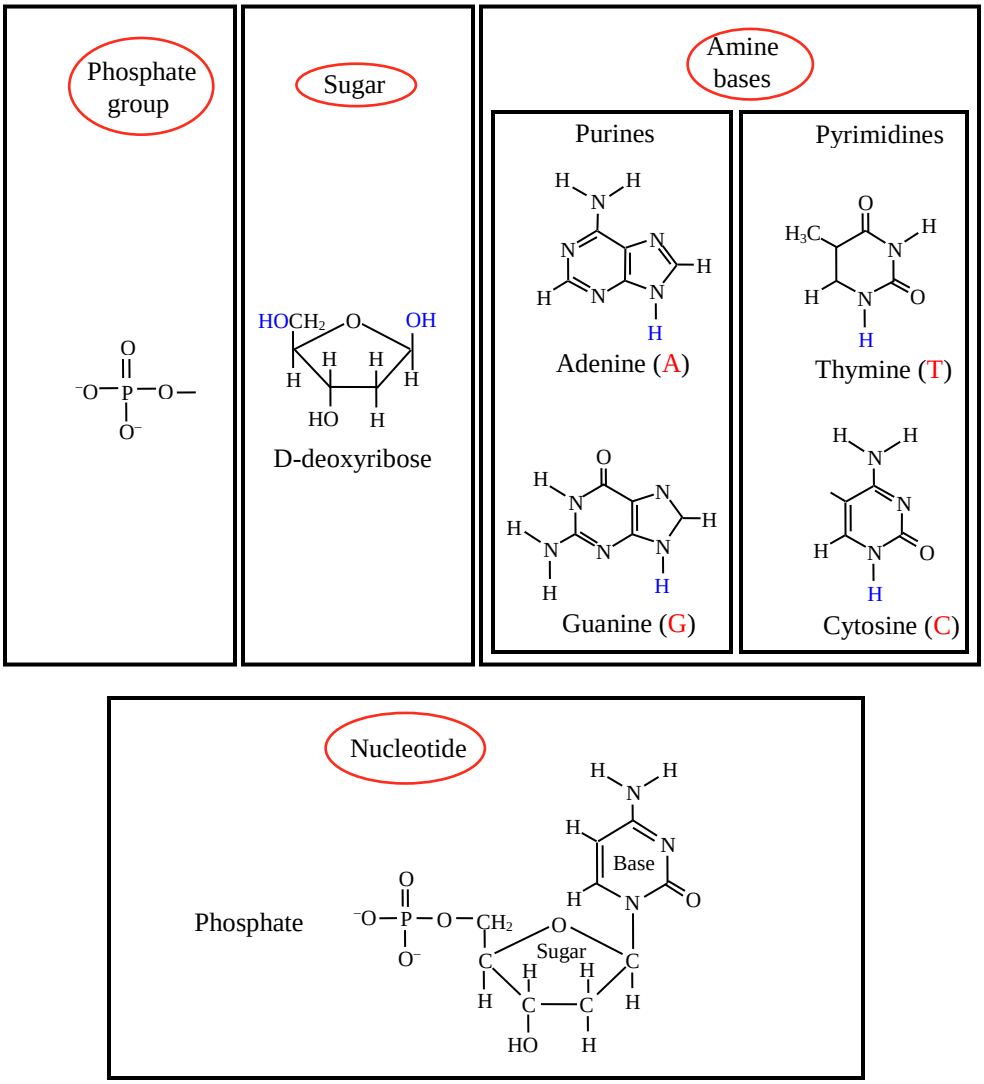

Figure 6: Components of the DNA molecule.

DNA of higher organisms folds into a double helix structure whereby the amine bases are stacked and hydrogen bonded. The pair A-T has two hydrogen bonds whereas the pair C-G has three hydrogen bonds. The two DNA chains forming the double helix run in opposite direction. Stacking of the amine bases and hydrogen bonding between them is the key driving force for the helix formation. Water hydrates the outside phosphate groups as well as produces hydrogen bonding between the base pairs.

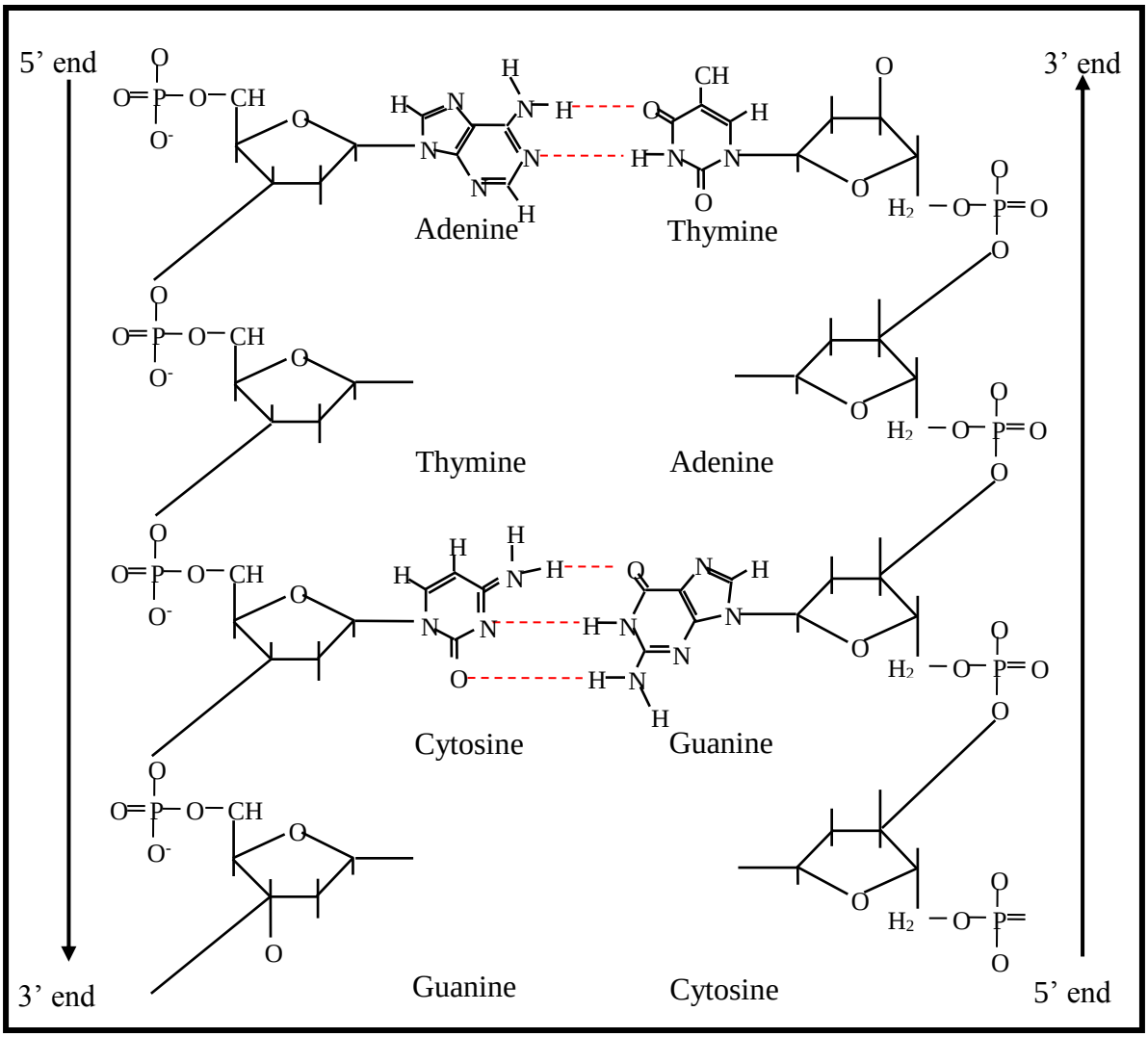

Figure 7: Amine base stacking and hydrogen bonding that form the DNA double helix.

X-ray diffraction helped in the determination of the precise structure of the DNA double helix. Information like the repeat distance per base pair (3.4 Å) and the helix pitch (34 Å) were determined.

THE DNA DOUBLE HELIX

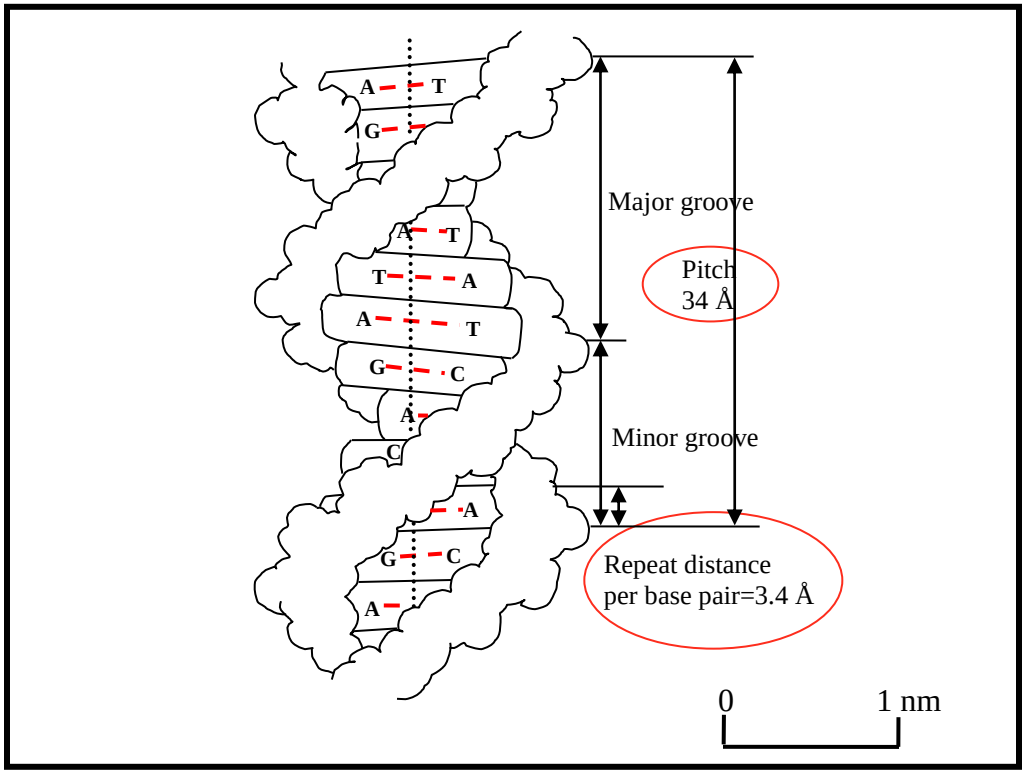

Figure 8: The DNA double helix. Structure for the dominant form of DNA (the B type) is schematically represented here.

4. PROTEINS

Proteins are responsible for the enzymatic (or catalytic), structural and regulatory functions of the cell. Most of the cell processes are mediated by proteins. Proteins are formed of polypeptide chains which are coiled and folded in a precise way dictated by the amino acid sequence. Unfolding (denaturation) leads to loss of biological activity. Each polypeptide consists of a specific amino acid sequence. No two long amino acid sequences are alike. Peptides are synthesized through a condensation reaction of two amino acids to form the amide (also called peptide) bond. A water molecule is a byproduct. Energy is provided for this chemical reaction. RNA plays the roles of messenger (mRNA), adapter or transfer (tRNA), and linker or ribosomal (rRNA) in order to transcribe the DNA code into a correct amino acid sequence.

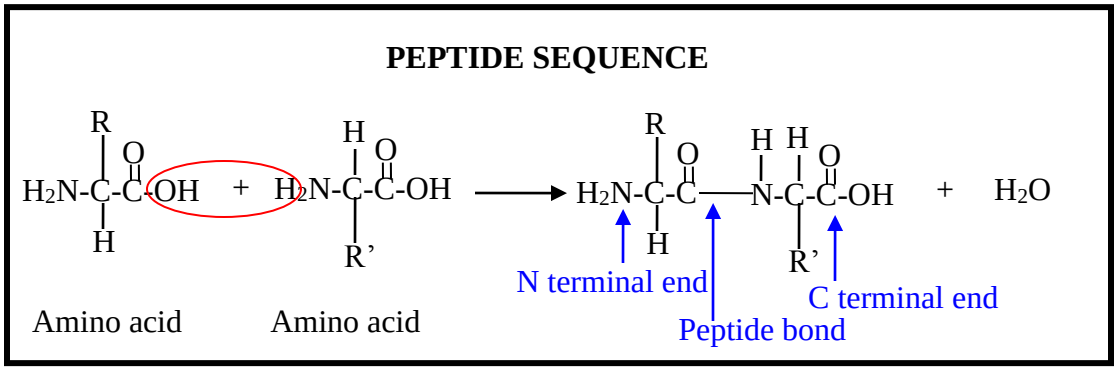

Figure 9: A peptide sequence of two amino acids.

There are 20 amino acids involved in protein synthesis. These consist of charged (hydrophilic) head groups and side chains which can be either polar (charged) or nonpolar (uncharged, hydrophobic). The hydrophobic groups tend to be buried in the middle of proteins out of contact with water.

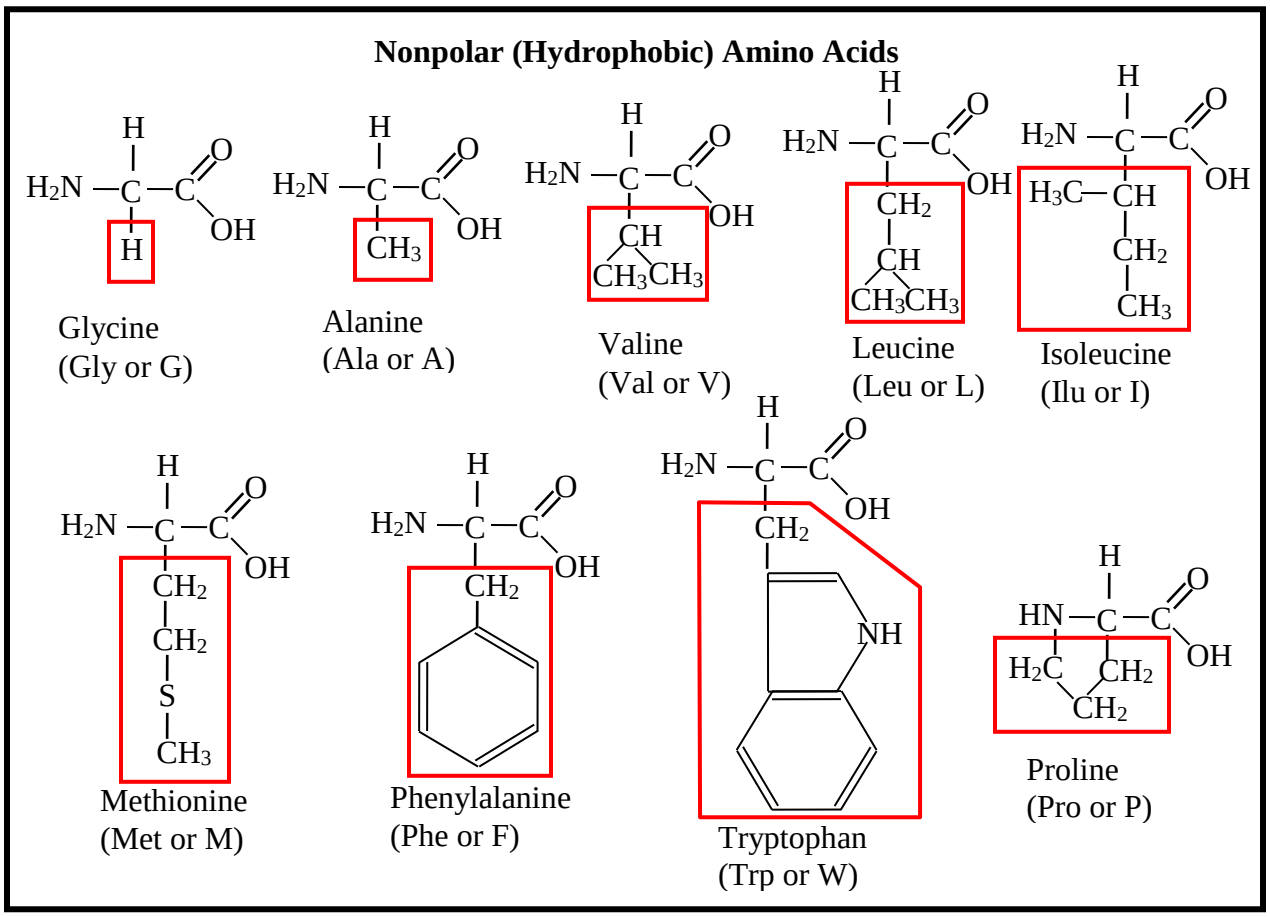

Figure 10a: The group of nonpolar (hydrophobic) amino acids.

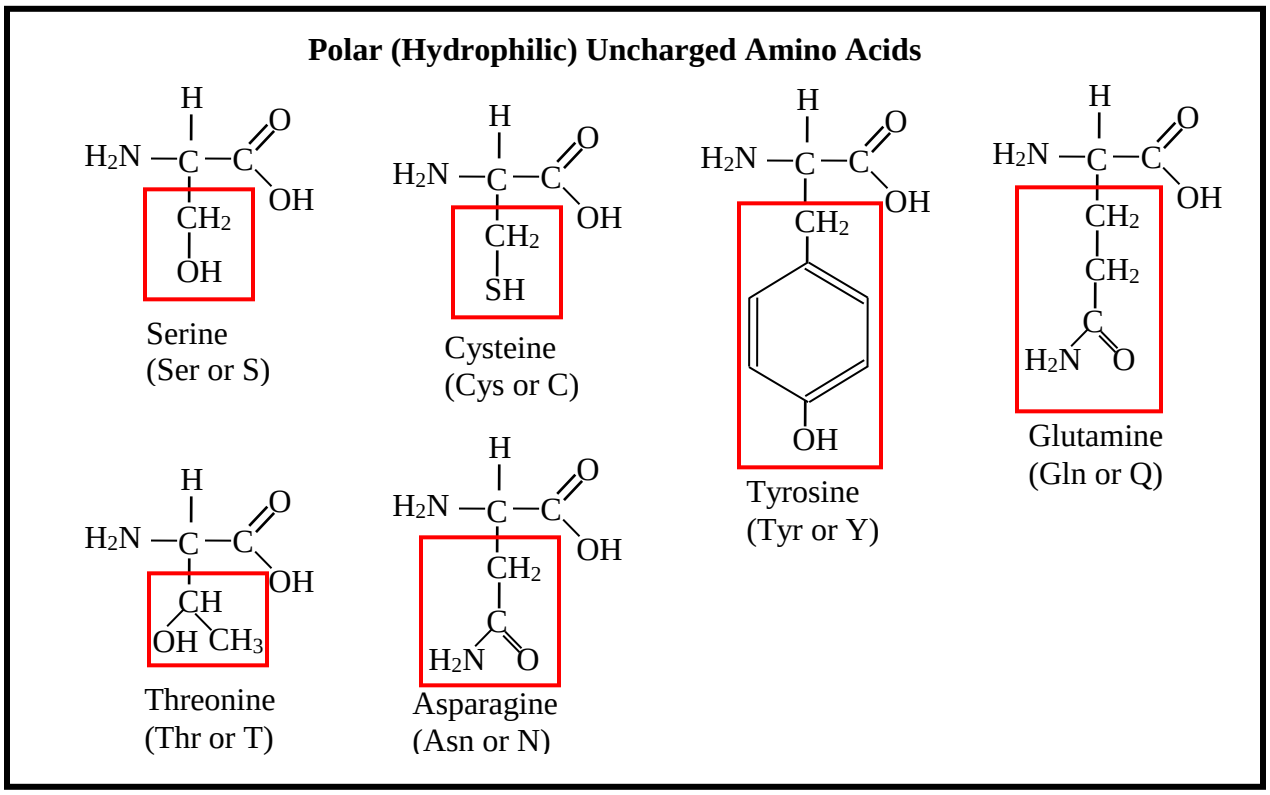

Figure 10b: The group of polar (hydrophilic) uncharged amino acids.

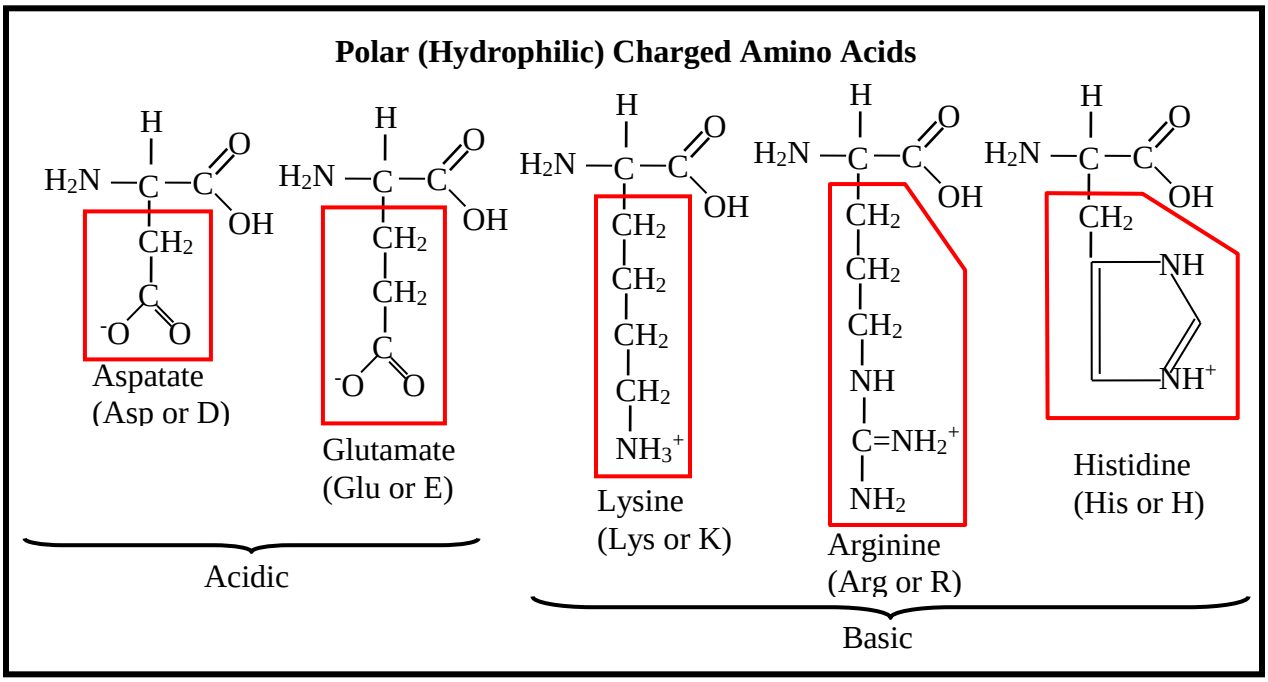

Figure 10c: The group of polar (hydrophilic) charged amino acids.

Molecular chaperones are needed in the folding of proteins in order to prevent incorrect molecular conformations. Proteins comprise four hierarchical self-assembling structures. These are the primary, secondary, tertiary and quaternary structures.

The primary structure refers to the amino acid sequence along the peptide chains. mRNA, tRNA and rRNA play the roles of transcribing, transferring and linking the amino acid sequence. The secondary folding structure is determined by the amino acid sequence and happens spontaneously under favorable environmental conditions. Folding occurs in the form of alpha helix and beta sheet while random coil corresponds to no folding. The alpha helix contains 3.6 amino acids per helical turn bridging the peptide bond of every fourth amino acid. For example, leucine forms alpha helices. The beta sheet is a planar structure involving –CO to HN– hydrogen bonds between two polypeptides. For example, valine forms beta sheets. Complex proteins require chaperone assistance in folding.

The tertiary structure involves interaction between the R groups of amino acids. Electrostatic, hydrophobic and hydrogen bonding interactions as well as S-S covalent bonds contribute to the structure formation. Polypeptides are folded, coiled and twisted into the desired protein's native configuration. A domain of 50 to 350 amino acids is required to fulfill a specific function. Some proteins consist of multiple functions played by multiple domains. The quaternary structure is made of two or more chains. Each chain can have two or more domains.

Information included in the DNA gene sequence (A, G, T, C bases) is used to set the amino acid sequence in protein synthesis. For example, an AAG sequence in a DNA strand (running from 5' to 3' positions) transcribes to an AAG sequence in the mRNA and contributes to the addition of Lys (lysine) amino acid in the polypeptide synthesis. The beginning (start) and end (stop) of a gene sequence are also included in the DNA code.

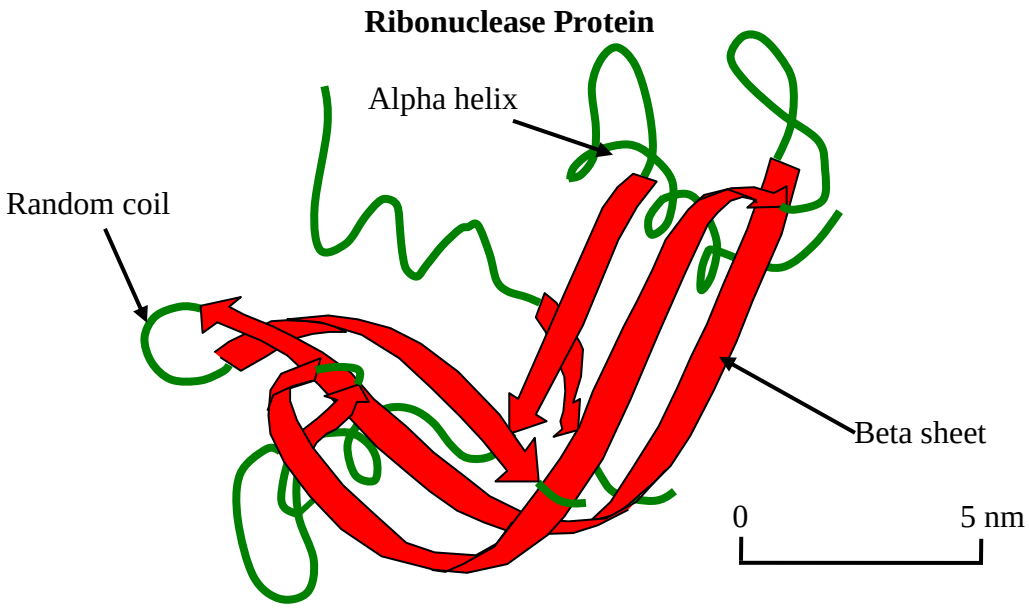

Figure 11: Schematic representation of Ribonuclease which is a globular protein containing beta sheet, alpha helix and random coil secondary structures. Ribonuclease is an enzyme that catalyzes the hydrolysis of RNA into smaller components.

5. POLYSACCHARIDES

Polysaccharides are polymers formed of monosaccharides (Greek for "single sugar") joined together by glycosidic bonds. There are two categories of sugars: the aldosugars and the ketosugars.

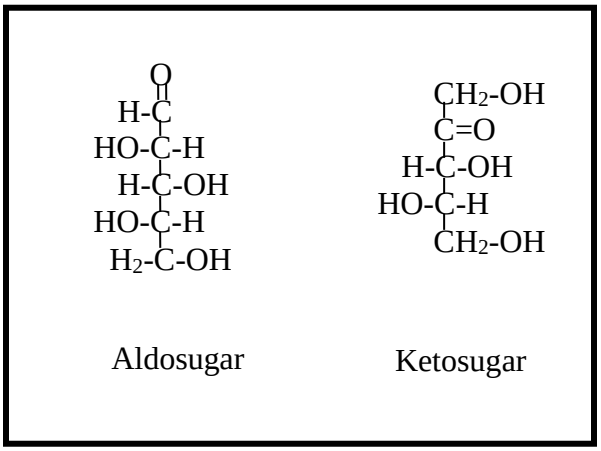

Figure 12: The two categories of sugar molecules

The most common form of aldosugar is the D-glucose ($C_6H_{12}O_6$) which occurs in linear and cyclic forms. The general formula $C_nH_{2n}O_n$ is characteristic of sugars. These are also referred to as carbohydrates.

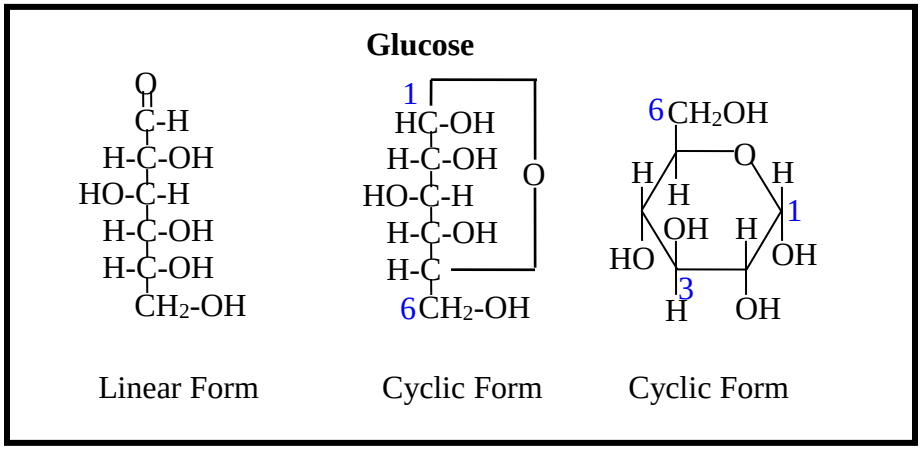

Figure 13: The linear and cyclic forms of D-glucose.

Two well-known polysaccharides in plant cells are starch and cellulose. Two well-known polysaccharides in animal cells are glycogen and chitin. Starch and glycogen contain alpha glycosidic bonds whereas cellulose and chitin contain beta glycosidic bonds. Polysaccharides are often branched and are represented by the chemical formula $(C_6H_{10}O_5)_n$ with n being a large number (hundreds to thousands).

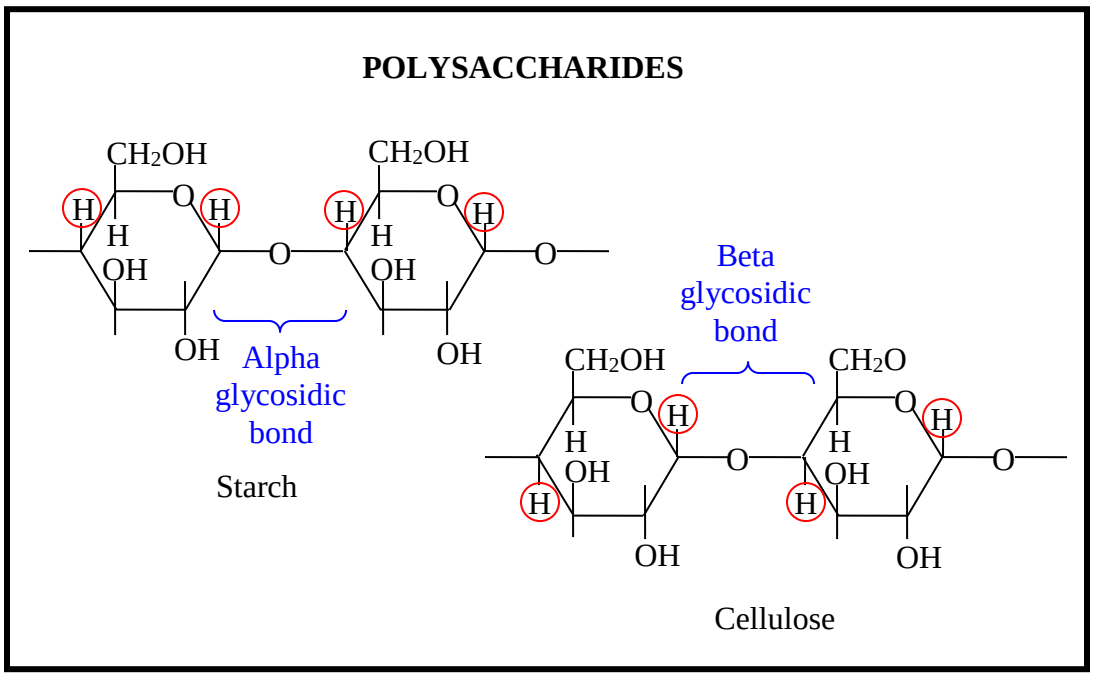

Figure 14: Chemical formulas for two plant polysaccharides.

Mammals do not possess enzymes that can hydrolyze the beta glycosidic bonds and cannot therefore digest cellulose.

6. CELLS AND ORGANELLES

The basic unit in biology is the cell. Eukaryotes are characterized by well defined membranes around the organelles (mitochondria, chloroplasts, inner cell membrane systems) as well as around the nucleus. In contrast, bacteria have no nucleus or organelles and are termed prokaryotes. Eukaryotes evolved from prokaryotes.

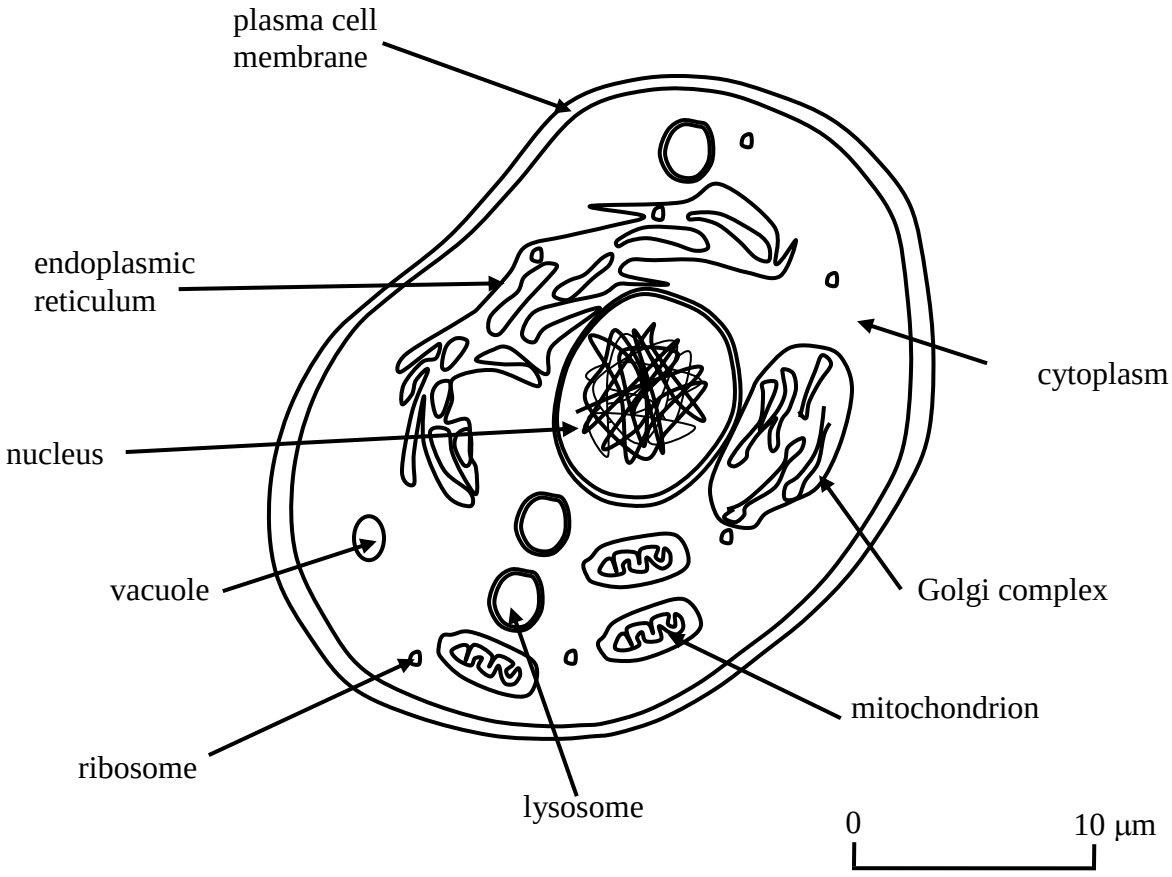

Figure 15: Schematic representation of an animal cell showing the various organelles.

A brief description of the various organelles is included here. These include the nucleus, the endoplasmic reticulum, the Golgi complex, the mitochondria, the lysosomes, the vacuoles and vesicles.

The cell nucleus contains the chromosomes where DNA is tightly packed. The nucleus is bounded by a double membrane that keeps its contents separate from the cytoplasm. Membrane pores allow the free movement of small molecules and ions. The movement of larger molecules such as proteins is controlled by specialized carrier proteins (enzymes)

The endoplasmic reticulum (ER) consists of an interconnected network of tubular membranes and vesicles and is the site of protein synthesis and transport. The ER is also the site for the sequestration of calcium and the production and storage of glycogen and steroids.

The Golgi complex serves in the processing and packaging of secretory proteins, in the synthesis of polysaccharides and in the processing of lipids.

Mitochondria play an important role in the oxidation of sugars which are the main source of energy for the cell. It is the site for the generation of adenosine triphosphate (ATP) which is the energy currency within the cell. The cell localizes most of the enzymes in the mitochondrion. Some proteins are synthesized in the mitochondria. In addition to being the energy production center, mitochondria are also involved in cell signaling, cell differentiation as well as cell growth. Mitochondria have their own DNA which is independent of the DNA in the nucleus.

Lysosomes contain digestive enzymes along with carbohydrates. The membrane surrounding the lysosome prevents the digestive enzymes from destroying the cell. Lysosomal proteins are made in the ER and Golgi apparatus. Peroxisomes play a role in breaking down fatty acids.

Vacuoles are used for temporary storage or transport. They remove and export unwanted substances, maintain the proper internal cell hydrostatic pressure and pH and enable cell flexibility. Vacuoles are important components of plant cells.

The cell contains many other components. Vesicles are used for storage. Plant cells contain chloroplasts where photosynthesis takes place. The cytoplasm contains tubules and filaments for flexibility and mobility of the cell. Chaperones help in the correct assembly of proteins. Enzymes are synthesized in the rough ER, packaged in the Golgi complex and released by vesicle transport.

7. CHARACTERIZATION METHODS

There are many characterization methods used in biology. Some of the routine techniques include: mass spectroscopy to measure molecular weights, circular dichroism (CD) to distinguish between coil, beta sheet and alpha helix configurations, Cryo-Transmission Electron Microscopy (TEM) to visualize down to the molecular level, Vis-UV absorption spectroscopy to detect the existence of DNA or proteins in the sample, Electrophoresis to determine fragment sizes, etc. For example, UV absorption spectroscopy is sensitive to π

bonding in the amine bases in DNA (260 nm line) and to the existence of Tryptophan amino acid in proteins (280 nm line). Wide-angle x-ray diffraction is used to determine crystalline structures. When crystalline bio-material cannot be obtained, small-angle x-ray scattering (SAXS) and small-angle neutron scattering (SANS) are used in order to determine amorphous structures. Dynamic Light Scattering (DLS) is also used to estimate particle sizes.

8. NEUTRON SCATTERING LENGTHS

Neutron scattering works best when deuteration is possible. Deuteration is achieved either by using a deuterated solvent or by deuterium labeling the macromolecules. Due to the complex "natural" processes involved, deuterium labeling is not easy to achieve in biology. Synthesis using deuterated amino acids is achieved for short polypeptide sequences of less than 100 amino acids. That process is complex and time consuming even with the use of automated equipment. Another more involved route for obtaining deuterated bio-macromolecules is to grow organisms in a d-water culture then separate the deuterated proteins.

Water is the solvent of choice in biology research since it is the major component in the cell. The dialysis process allows the exchange of H by D and vice versa. This helps enhance the neutron contrast and helps deuterium exchange on the macromolecules. C-H bonds do not exchange but O-H and N-H bonds exchange into O-D and N-D.

The tabulated values for the scattering lengths of the light chemical elements found in proteins and DNA are included:

$b_H = -3.739*10^{-13}$ cm, $b_D = 6.671*10^{-13}$ cm, $b_C = 6.646*10^{-13}$ cm
$b_O = 5.803*10^{-13}$ cm, $b_P = 5.130*10^{-13}$ cm, $b_S = 2.847*10^{-13}$ cm.

The scattering lengths, densities and molecular volumes for water and d-water are:

$b_{H_2O} = -1.675*10^{-13}$ cm, $b_{D_2O} = 19.145*10^{-13}$ cm
$d_{H_2O} = 1$ g/cm^3, $d_{D_2O} = 1.11$ g/cm^3
$v_{H_2O} = 29.9$ Å^3, $v_{D_2O} = 29.9$ Å^3

The scattering length densities are given by:

$$\rho_{H_2O} = \frac{b_{H_2O}}{v_{H_2O}} = -5.702*10^{-7}\ \text{Å}^{-2}, \quad \rho_{D_2O} = \frac{b_{D_2O}}{v_{D_2O}} = 6.403*10^{-6}\ \text{Å}^{-2}$$

A table summarizes the chemical formulas, the scattering lengths and scattering length densities for the various amino acids (Jacrot, 1976). Four cases are considered: (1) the case of hydrogenated molecules (amino acids or nucleotides), (2) the case of hydrogenated molecules with H/D exchange, (3) the case of deuterated molecules, and

(4) the case of deuterated molecules with D/H exchange. The same information is included for the DNA and the RNA nucleotides These numbers are estimates for thermal neutron scattering and will vary with neutron wavelength and solution conditions (such as pH, etc).

Table 1: Scattering lengths for amino acids and deuterated amino acids after H/D or D/H exchange. Scattering lengths for nucleotides and deuterated nucleotides are also included.

Name	H/D Content	Formula	Scattering Length (10^{-12} cm)	Density (g/cm^3)	Scattering Length Density (10^{-6} $Å^{-2}$)
Amino Acids					
Glycine (Gly or G)	Hydrogenated	C_2NOH_3	1.72	1.43	2.60
	H/D Exchange	C_2NOH_2D	2.77	1.45	4.16
	Deuterated	C_2NOD_3	4.85	1.50	7.30
	D/H Exchange	C_2NOHD_2	3.81	1.48	5.73
Alanine (Ala or A)	Hydrogenated	C_3NOH_5	1.64	1.29	1.79
	H/D Exchange	C_3NOH_4D	2.68	1.31	2.93
	Deuterated	C_3NOD_5	6.85	1.38	7.48
	D/H Exchange	C_3NOHD_4	5.80	1.36	6.34
Valine (Val or V)	Hydrogenated	C_5NOH_9	1.47	1.16	1.04
	H/D Exchange	C_5NOH_8D	2.52	1.17	1.78
	Deuterated	C_5NOD_9	10.84	1.27	7.65
	D/H Exchange	C_5NOHD_8	9.80	1.25	6.92
Leucine (Leu or L)	Hydrogenated	C_6NOH_{11}	1.39	1.12	8.28
	H/D Exchange	$C_6NOH_{10}D$	2.43	1.13	1.45
	Deuterated	C_6NOD_{11}	12.84	1.23	7.65
	D/H Exchange	C_6NOHD_{10}	11.80	1.22	7.03
Isoleucine (Ilu or I)	Hydrogenated	C_6NOH_{11}	1.39	1.11	8.24
	H/D Exchange	$C_6NOH_{10}D$	2.43	1.12	1.44
	Deuterated	C_6NOD_{11}	12.84	1.22	7.61
	D/H Exchange	C_6NOHD_{10}	11.80	1.21	6.99
Phenylalanine (Phe or F)	Hydrogenated	C_9NOH_9	4.13	1.20	2.03
	H/D Exchange	C_9NOH_8D	5.17	1.21	2.54
	Deuterated	C_9NOD_9	13.50	1.27	6.64
	D/H Exchange	C_9NOHD_8	12.46	1.27	6.13

Tyrosine (Tyr or Y)	Hydrogenated	$C_9NO_2H_9$	4.71	1.33	2.31
	H/D Exchange	$C_9NO_2H_7D_2$	6.79	1.35	3.34
	Deuterated	$C_9NO_2D_9$	14.08	1.40	6.92
	D/H Exchange	$C_9NO_2H_2D_7$	12.00	1.39	5.89
Tryptophan (Trp or W)	Hydrogenated	$C_{11}N_2OH_{10}$	6.02	1.30	2.54
	H/D Exchange	$C_{11}N_2OH_8D_2$	8.11	1.32	3.41
	Deuterated	$C_{11}N_2OD_{10}$	16.43	1.37	6.92
	D/H Exchange	$C_{11}N_2OH_2D_8$	14.35	1.36	6.04
Aspartate (Asp or D)	Hydrogenated	$C_4NO_3H_4$	3.84	1.67	3.38
	H/D Exchange	$C_4NO_3H_3D$	4.88	1.68	4.30
	Deuterated	$C_4NO_3D_4$	8.00	1.73	7.05
	D/H Exchange	$C_4NO_3HD_3$	6.96	1.71	6.13
Glutamate (Glu or E)	Hydrogenated	$C_5NO_3H_6$	3.76	1.51	2.67
	H/D Exchange	$C_5NO_3H_5D$	4.80	1.52	3.41
	Deuterated	$C_5NO_3D_6$	10.00	1.58	7.11
	D/H Exchange	$C_5NO_3HD_5$	8.96	1.57	6.37
Serine (Ser or S)	Hydrogenated	$C_3NO_2H_5$	2.22	1.46	2.24
	H/D Exchange	$C_3NO_2H_3D_2$	4.30	1.49	4.34
	Deuterated	$C_3NO_2D_5$	7.43	1.54	7.49
	D/H Exchange	$C_3NO_2H_2D_3$	5.34	1.51	5.39
Threonine (Thr or T)	Hydrogenated	$C_4NO_2H_7$	2.14	1.37	1.75
	H/D Exchange	$C_4NO_2H_5D_2$	4.22	1.40	3.46
	Deuterated	$C_4NO_2D_7$	9.43	1.47	7.72
	D/H Exchange	$C_4NO_2H_2D_5$	7.34	1.44	6.01
Asparagine (Asn or N)	Hydrogenated	$C_4N_2O_2H_6$	3.45	1.40	2.55
	H/D Exchange	$C_4N_2O_2H_3D_3$	6.57	1.44	4.86
	Deuterated	$C_4N_2O_2D_6$	9.69	1.47	7.17
	D/H Exchange	$C_4N_2O_2H_3D_3$	6.57	1.44	4.86
Glutamine (Gln or Q)	Hydrogenated	$C_5N_2O_2H_8$	3.36	1.32	2.09
	H/D Exchange	$C_5N_2O_2H_5D_3$	6.49	1.35	4.03
	Deuterated	$C_5N_2O_2D_8$	11.69	1.40	7.26
	D/H Exchange	$C_5N_2O_2H_3D_5$	8.57	1.37	5.32
Lysine (Lys or K)	Hydrogenated	$C_6N_2OH_{13}$	1.58	1.22	8.96
	H/D Exchange	$C_6N_2OH_9D_4$	5.74	1.25	3.26
	Deuterated	$C_6N_2OD_{13}$	15.11	1.34	8.58
	D/H Exchange	$C_6N_2OH_4D_9$	10.95	1.30	6.21

Arginine (Arg or R)	Hydrogenated	$C_6N_4OH_{13}$	3.45	1.44	1.91
	H/D Exchange	$C_6N_4OH_8D_5$	9.70	1.50	5.36
	Deuterated	$C_6N_4OD_{13}$	16.984	1.56	9.39
	D/H Exchange	$C_6N_4OH_5D_8$	10.74	1.51	5.94
Histidine (His or H)	Hydrogenated	$C_6N_3OH_7$	4.96	1.36	2.84
	H/D Exchange	$C_6N_3OH_5D_2$	6.84	1.38	4.09
	Deuterated	$C_6N_3OD_7$	12.05	1.43	7.20
	D/H Exchange	$C_6N_3OH_2D_5$	9.96	1.41	5.96
Methionine (Met or M)	Hydrogenated	C_5NOSH_9	1.76	1.28	1.03
	H/D Exchange	C_5NOSH_8D	2.80	1.29	1.64
	Deuterated	C_5NOSD_9	11.13	1.36	6.52
	D/H Exchange	C_5NOSHD_8	10.09	1.35	5.91
Cysteine (Cys or C)	Hydrogenated	C_3NOSH_5	1.93	1.62	1.82
	H/D Exchange	$C_3NOSH_3D_2$	4.00	1.65	3.79
	Deuterated	C_3NOSD_5	7.13	1.70	6.75
	D/H Exchange	$C_3NOSH_2D_3$	5.05	1.67	4.78
Proline (Pro or P)	Hydrogenated	C_5NOH_7	2.22	1.25	1.72
	H/D Exchange	C_5NOH_7	2.22	1.25	1.72
	Deuterated	C_5NOD_7	9.51	1.34	7.36
	D/H Exchange	C_5NOD_7	9.51	1.34	7.35

DNA Nucleotides

Adenine	Hydrogenated	$PN_5O_5C_{10}H_{11}$	10.63
	H/D Exchange	$PN_5O_5C_{10}H_9D_2$	12.71
	Deuterated	$PN_5O_5C_{10}D_{11}$	22.08
	D/H Exchange	$PN_5O_5C_{10}H_2D_9$	20.00
Guanine	Hydrogenated	$PN_5O_6C_{10}H_{11}$	11.21
	H/D Exchange	$PN_5O_6C_{10}H_8D_3$	14.33
	Deuterated	$PN_5O_6C_{10}D_{11}$	22.66
	D/H Exchange	$PN_5O_6C_{10}H_3D_8$	19.54
Cytosine	Hydrogenated	$PN_3O_6C_9H_{11}$	8.67
	H/D Exchange	$PN_3O_6C_9H_9D_2$	10.75
	Deuterated	$PN_3O_6C_9D_{11}$	20.12
	D/H Exchange	$PN_3O_6C_9H_2D_9$	18.04

Thymine	Hydrogenated	$PN_2O_7C_{10}H_{12}$	8.61
	H/D Exchange	$PN_2O_7C_{10}H_{11}D_1$	9.65
	Deuterated	$PN_2O_7C_{10}D_{12}$	21.10
	D/H Exchange	$PN_2O_7C_{10}H_1D_{11}$	20.06

RNA Nucleotides

Adenine	Hydrogenated	$PN_5O_6C_{10}H_{11}$	11.21
	H/D Exchange	$PN_5O_6C_{10}H_8D_3$	14.33
	Deuterated	$PN_5O_6C_{10}D_{11}$	22.66
	D/H Exchange	$PN_5O_6C_{10}H_3D_8$	19.54
Guanine	Hydrogenated	$PN_5O_7C_{10}H_{11}$	11.79
	H/D Exchange	$PN_5O_7C_{10}H_7D_4$	15.95
	Deuterated	$PN_5O_7C_{10}D_{11}$	23.24
	D/H Exchange	$PN_5O_7C_{10}H_4D_7$	19.08
Cytosine	Hydrogenated	$PN_3O_7C_9H_{11}$	9.25
	H/D Exchange	$PN_3O_7C_9H_8D_3$	12.37
	Deuterated	$PN_3O_7C_9D_{11}$	20.70
	D/H Exchange	$PN_3O_7C_9H_3D_8$	17.58
Uracil	Hydrogenated	$PN_2O_8C_9H_{10}$	9.27
	H/D Exchange	$PN_2O_8C_9H_8D_2$	11.35
	Deuterated	$PN_2O_8C_9D_{10}$	19.68
	D/H Exchange	$PN_2O_8C_9H_2D_8$	17.60

Note that the density of nucleotides is estimated to be between 1.73 g/cm^3 and 1.78 g/cm^3. This gives scattering length densities for hydrogenated nucleotides between $3.18*10^{-6}$ Å^{-2} and $3.66*10^{-6}$ Å^{-2}.

A figure summarizes the average scattering length densities (ρ = b/v where b is the scattering length and v is the molecular volume) values for hydrogenated proteins and DNA without H/D exchange (left axis) and with H/D exchange (right axis). Average values for deuterated proteins and deuterated DNA without and with D/H exchange are also included (Jacrot, 1976).

Note that the neutron contrast $\Delta\rho^2$ is defined as the difference in scattering length densities (squared) between the macromolecules (proteins or DNA) and the solvent (water). The average scattering length density for hydrogenated proteins is $1.8*10^{-6}$ Å^{-2} (left axis) whereas after H/D exchange (in D_2O) it is $3*10^{-6}$ Å^{-2} (right axis). For example, proteins are contrast matched in mixtures of 40 % D_2O and 60 % H_2O, DNA is contrast

matched for 65 % D_2O and 35 % H_2O, lipids are contrast matched for 15 % D_2O and 85 % H_2O and polysaccharides are contrast matched for 30 % D_2O and 70 % H_2O.

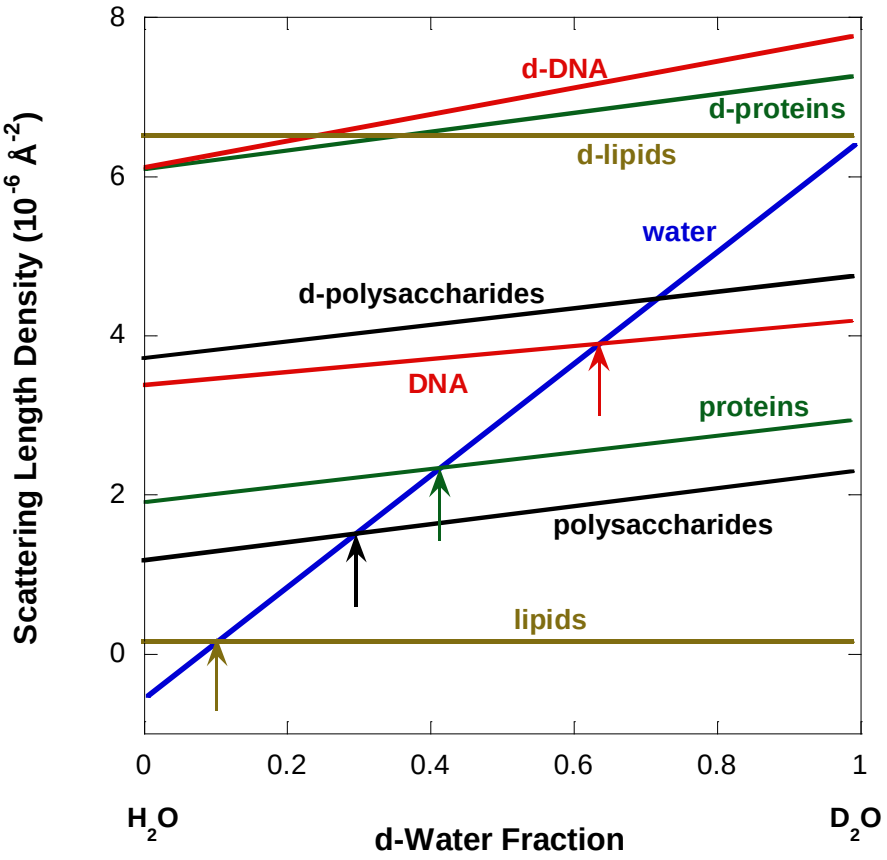

Figure 16: Average scattering length densities for DNA, proteins, lipids and polysaccharides as well as deuterated DNA, deuterated proteins, deuterated lipids and deuterated polysaccharides following H/D exchange in H_2O (left) or D_2O (right). Arrows mark the D_2O/H_2O contrast match conditions.

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QUESTIONS

1. What are biological membranes made out of?
2. What is a condensation reaction? Where do condensation reactions take place?

3. What are the main components of DNA? How many amine bases are there? Name them.
4. What is the difference between DNA and RNA?
5. What are the main conformations of proteins?
6. How many amino acids are used in the synthesis of proteins?
7. How is the genetic DNA code used for the synthesis of proteins?
8. What is the prominent component of polysaccharides? Name a couple of polysaccharides.
9. Which cell organelle is the center of energy production?
10. How is dialysis used to enhance the neutron contrast?

ANSWERS

1. Biological membranes (those found in living organisms) contain lipids, but also proteins and their glycosylated derivatives. Lipids consist of hydrophilic heads and hydrophobic tails. Lipids are produced through the condensation reaction of glycerol and a fatty acid group.
2. A chemical reaction is referred to as a "condensation reaction" when it produces a water molecule. Condensation reactions occur during the synthesis of lipids, of DNA and of proteins.
3. DNA is formed of phosphate groups, sugars and amine bases. There are four amine bases. These are Adenine (A), Thymine (T), Guanine (G) and Cytosine (C).
4. The main difference between DNA and RNA is in the sugar group. DNA contains deoxyribose whereas RNA contains ribose. Moreover, in RNA, Thymine is replaced by Uracil (U).
5. Protein conformations are the alpha helix, the beta sheet and the random coil.
6. There are 20 amino acids involved in the synthesis of proteins.
7. The sequence of three nucleotides codes for the addition of a specific amino acid in the synthesis of a peptide sequence.
8. Polysaccharides are made through the polymerization of sugars. Starch and cellulose are plant polysaccharides. Glycogen and chitin are animal polysaccharides.
9. The mitochondrion is the center of energy production. Energy is produced through the oxidation mainly of sugars.
10. A dialysis bag (containing the macromolecules) is used inside a container full of d-water in order to enhance deuterium exchange. This results in partially deuterated macromolecules (DNA or proteins) by deuterium exchange on O and N atoms. Dialysis is sometime performed more than once in order to enhance the deuteration level.